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(54) Multi-probe system

(57) A multi-lumen, multi-functional catheter (2) system comprising a plurality of axial lumens (6,8,10,12,14,16), at least one lumen supporting a functionality other than material delivery and material removal.

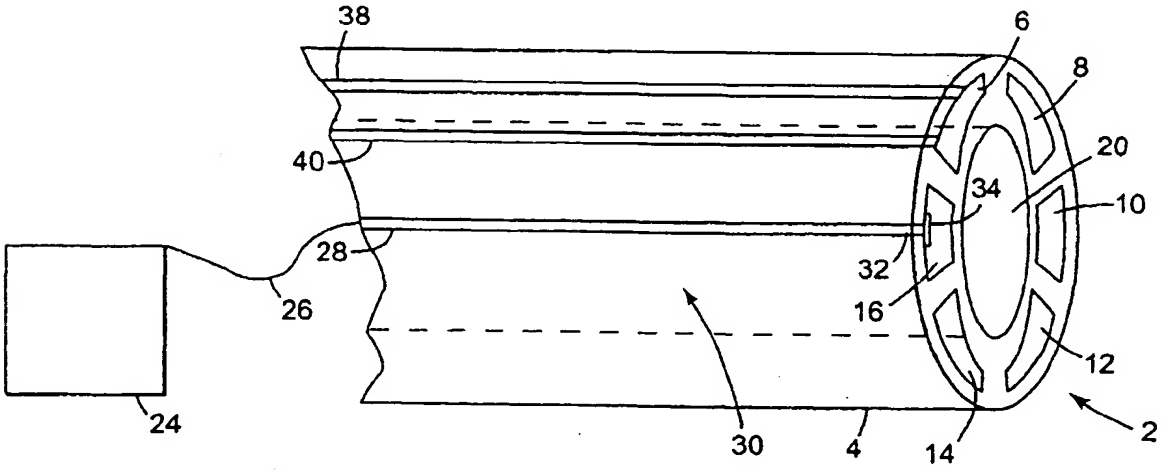

Fig. 1

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Description

[0001] This invention relates to an apparatus and method for catheterization of the tissues and fluid spaces, including blood vessels, of the human body. The invention also relates to the method by which diagnostic and therapeutic agents and/or procedures may be delivered to any of those body parts or regions. In particular, the present invention relates to the design and use of a multi-lumen catheter for providing multiple, and not necessarily complimentery functions, such as sampling of the fluids within the extracellular and interstitial spaces of the brain, spinal cord, or other body tissues, concurrently with drug delivery, electrical recording / stimulating, or the delivery of any other type of therapy into the same tissues in accordance with the need for such therapies.

[0002] Surgical procedures, especially neurosurgical procedures that involve open craniotomy, carry an intrinsically high level of risk of infection and hemorrhage. A variety of new techniques aimed at minimizing the invasiveness of interventional procedures have been introduced in the hope of reducing the surgical risk and shorten a patient's hospital stay and overall rehabilitation. Placement of probes and catheters into the brain using stereotactic and image-guided procedures provides one means of minimizing these risks. However, many types of interventional procedures, including those that require drug delivery into the brain, sometimes require either catheterization at multiple target points, or subsequent re-implantation of the catheter to optimize the therapy being delivered to the brain.

[0003] Current methods of catheterization of the parenchymal tissues of the brain make it possible to measure intracranial pressure (U.S. Patent No. 5,107,847), deliver drugs in a rate-controlled manner (U.S. Patent No. 5,836,935), infuse various substances into the brain (U.S. Patent No. 5,720,720), and convey fluids out of the brain (U.S. Patent No. 5,772,625). Very recent technological developments are now leading to intraparenchymal catheterization systems that can be positioned within the brain by magnetic stereotaxis (U.S. Patent Nos. 5,125,888; 5,707,335; 5,779,694), that are visible under magnetic resonance (MR) imaging (U.S. Patent No. 6,026,316), and that contain multi-purpose electrodes (U.S. Patent No. 5,843,093). In addition, there are several types of implantable neurostimultor devices that have been disclosed. These include those described by Otten (U.S. Patent No. 5,344,439), Hess et al. (U.S. Patent No., 4,800,898), and Tarjan et al. (U.S. Patent No. 4,549,556) as three examples thereof. However, none of the available methods of intraparenchymal catheterization can carry out multiple input-output functions at the same time with the same implanted device. With the exception of the method taught by Otten (U.S. Patent No. 5,344,439), an already implanted device or part of an implanted device must be withdrawn before another probe is subsequently inserted into the tissue to perform additional functions. U.S. patent No. 5,788,713 describes the availability of both a delivery lumen and sampling lumen on a single catheter system.

[0004] The inventors have determined that it is increasingly important to determine other local characteristics of the region where active materials are delivered that can effect the efficacy or optimization of the treatment, such as pH, osmololity, viscosity, electrolyte content, temperature, fluid flow rates, and concentrations of specific ingredients. No present systems enable both the delivery of therapeutic materials and the measurement of significant local properties (except for the single noted instance oif delivery and physical sampling).

[0005] U.S. Pat. 4,114,606 discloses a monitoring apparatus for intracranial pressure measurement, wherein electromagnetic radiation is imposed on a passive circuit implanted in the cranium, the frequency at which the radiation is absorbed reflecting intracranial pressure. U. S. Pat. 4,147,161 to Ikebe, et al. discloses a system for measuring or monitoring intracranial pressure which comprises a non-elastic detecting pouch inserted between the skull and the brain, wherein a pressure measuring device in the liquid in the pouch indirectly measures the intracranial pressure. U.S. Pat. 4,156,422 to Hildebrandt discloses an apparatus for treating hydrocephalus comprising a housing which contains subcutaneously implantable components for measuring and controlling fluid pressure, wherein a second housing outside the patient contains measuring and control components whereby an intracerebral space may be automatically drained in response to a predetermined adjustable ICP.

[0006] U.S. Pat. 4,210,029 to Porter discloses a differential sensor unit utilizing fiber optic light guides, wherein three light guides pass within a pneumatic line into one end of a rigid cylindrical envelope implanted in the skull. Detectors are arranged to actuate pressure display and pneumatic controls to adjust the internal pressure of the envelope to match the ICP and thereby measure the ICP. U.S. Pat. 4,265,252 to Chubbuck discloses an implantable transensor device containing a passive RF resonant circuit which is responsive to changes in ICP. US Pat. 4,385,636 to Cosman discloses an implantable telemetric differential pressure sensing device comprising a planar closed conductive loop which moves with a flexible diaphragm, wherein the resonant frequency of the conductive loop is detected telemetrically to determine pressure in a body compartment.

[0007] Guidewires for the catheter or drug delivery system are usually made of radiopaque material so that their precise location can be identified during a surgical procedure through fluoroscopic viewing. Exemplary of guidewires used under X-ray viewing is the guidewire disclosed by LeVeen, U.S. Pat. No. 4,448,195, in which a radiopaque wire can be identified on fluoroscopic images by metered bands placed at predetermined locations. U.S. Pat. No. 5,375,596 to Twiss et al. discloses

a method for locating catheters and other tubular medical devices implanted in the human body using an integrated system of wire transmitters and receivers.

[0008] U.S. Pat. No. 5,325,865 to Beckman, et al. discloses a catheter assembly for measuring fluid pressure in a body cavity, comprising an optical converter responsive to an electrical power source for energizing a light-emitting diode which has drift characteristics which vary in response to temperature, and a detection circuit.

[0009] U.S. Pat. No. 5,843,093 to Howard discloses a dual purpose neuron-monitoring electrode assembly particularly suited for performing magnetic pallidotomy for the treatment of Parkinson's disease. However, unlike the present invention, the patent to Howard does not provide for an MR-compatible, multi-lumen probe which is capable ofcontaining several different internal devices that can sample the extracellular environment and react to it.

[0010] U.S. Pat. No. 5,843,150 to Dreessen, et al. discloses a system and method for providing electrical and/or fluid treatment within a patient's brain, wherein the device is an implantable device comprising a lumen, a catheter, an electrode, and a pump. However, unlike the present invention, thc patent to Dreessen, et al. does not provide for an MR-compatible, multi-lumen probe capable of containing several different internal devices that can sample the extracellular environment and react to it.

[0011] U.S. Pat. No. 5,843,148 to Gijsbers, et al. discloses a brain stimulation lead and multiple electrodes for precise delivery of electrical stimuli to a patient's brain.

[0012] U.S. Pat. No. 5,820,589 to Torgerson, et al. discloses an implantable medical pump comprising a fluid reservoir, a passive regulator assembly, an electromechanical controls means, and a means for receiving radio frequency signals to operate the electromechanical control means.

[0013] U.S. Pat. No. 5,858,009 to Jonkman discloses a multi-lumen cannula for conducting fluid to and from a body region, especially in left-heart and right-heart assist cardiac surgical procedures, wherein the septum separating the first and second catheter lumens is wire-reinforced to resist deflection of the septum.

[0014] A multi-lumen catheter system with novel forms and functions is disclosed. A desirable design feature for practice of this invention comprises an elongate element, such as a central barrel of a catheter which is surrounded by (or including within a major lumen) additional lumens which perform or transport various functions. In one embodiment that is particularly useful for therapy of the parenchymal tissues of the brain, one or more of the plurality of lumens around the central barrel are configured for sampling of fluids within the interstitial space (e.g., semiconductor based, microdialysis-based, electronically based, electrically based, interactance and transmittal, etc. sampling). Other lumens of the multi-lumen probe can be used for the delivery of drugs, therapeutic agents, diagnostic agents or view-enhancing agents into the parenchymal tissues, either via efflux from a single drug delivery lumen or via a multi-port configuration to facilitate broad spatial distribution ofthe drug within the tissue. In this embodiment, the central lumen can be used for any treatment or function, but especially either microdialysis or drug delivery, or it can be configured to accommodate a recording or stimulating electrode, such as a multi-purpose stereotactically placed electrode (e.g., U.S. Pat. No. 5,843,093). In a method of the invention, additional probes or devices that might be passed through either the central barrel of the catheter or through one of the surrounding ports include intracranial pressure probes, optical fibers and/or optical fiber bundles configured for conveying illumination and/or optical signals to and from the target tissues, iontophoresis probes, thermometry probes, blood-flow-sensing probes, chemical probes, sensing devices (even audio sensing devices, pressure-sensing devices, pH sensing devices, viscosity or osmololity sensing devices, radiation-sensing device, light-sensing device, etc.), vacuum lines, fluid delivery tubes and conduits, guidewires, fixed and adjustable-tipped steering probes and wires, electric field and magnetic field-sensing probes, electrodes and applicators, gene analysis chips and "lab-on-a-chip" structures, biopsy devices, tissue and cell implantation devices, cryogenic probes, thermal probes, ablation probes, cauterizing probes and tips, stents, coils, angioplasty balloons and devices, radioactive sources, magnetic and electric field sources, integrated circuits and electronic devices.

[0015] The unique compound nature of the catheter invention makes it possible to carry out several diagnostic and therapeutic tasks concurrently, with or without additional functional coupling between the processes. An important attribute of the medical device disclosed by this invention is to optimize the therapeutic response to the patient's clinical condition by using the sampling capabilities of the microdialysis or other diagnostic components of the catheter to provide information on the metabolic state of the target tissue (especially the brain) via analysis of the fluids within the extra-cellular matrix. Drug delivery into the parenchymal tissues can then be carried out via positive pressure infusion, or by diffusion-based delivery of pharmacological agents via the microdialysis process, using available lumens within the catheter to carry out either form oftreatment. In parallel with drug delivery, electrostimulation of the same or nearby target tissues/neurons can be carried out via a recording/stimulating electrode passed down a central or radially disposed barrel of the device.

In a method of the invention, a feedback mechanism may be used to automate and optimize the entire process, wherein a number of physiological variables can be taken into account by an algorithm that governs the therapeutic response of the catheter system. In another embodiment, physiological and metabolic data on the status ofthe patient (derived form other sensors on/in the

body, such as, for example, probes which monitor tissue oxygen levels, blood pH, concentration ofmaterials in the blood, blood flow, and other physiologic parameters) can be incorporated into the algorithm's treatment optimization process. Thus, for example, if a stroke or brain-injury patient were in an intensive care unit or other hospital bed setting, the vital-signs data from patient monitoring systems (including, in particular, intracranial pressure measurements) could be monitored by the system's signal processor, wherein the resulting information provided feedback control of the rates of drug flow into the brain. In another embodiment of the method of the invention, the microdialysis systems of the catheter device are used to sample endorphin levels, wherein the catheter's signal processor could then provide feedback control of the electrostimulation process so as to attenuate the effects of chronic pain.

[0016] In another embodiment of the method of the invention, the algorithm governing the patient's therapy preferably utilizes proportional-integral-derivative (PID) control functions, adaptive control functions, nonlinear control functions, multi-variable/state-space control functions, stochastic control functions and/or any other functional approach deemed appropriate for the implementation of the therapy. In all such cases, the controller could be designed to respond to changes in the patient's condition using artificial intelligence techniques that would let the feedback mechanism "learn" the best way to respond to changes in the patient's physiological or anatomical status. Such techniques might employ, among other things, "fuzzy logic" algorithms that can function in the presence of incomplete or indeterminate data.

[0017] A summary of the present invention includes at least a multi-lumen, multi-functional catheter system comprising a plurality of axial lumens, at least one lumen supporting a functionality other than material delivery and material removal. At least two individual lumens may be parallel to a central barrel of the catheter, and at least one of the at least two lumens may be used for sampling fluids in a body part into which the catheter is inserted. At least one ofthe axial lumens may be used for infusion, injection or other mechanism of delivery of diagnostic and/or therapeutic agents into a body part in which the catheter is inserted. The central lumen of the catheter may contain an electrode, such as a neurostimulator or radiofrequency-ablation lead.

An outer surface ofthe catheter may comprise a continuous sheath inside of which are located individual lumens, a central barrel and other functional components of the catheter system. At least some of said other function components may comprise electrical leads. There does not have to be an envelope around the catheter system, so there need not be any exterior covering element over the at least two lumens, a central barrel and other functional components of the catheter system. It is expected that at least one biological or physiological measuring device is present within at least one lumen. Such a biological or physiological measuring device would be expected to be connected to a signal receiving device by an electrical lead associated with the catheter system. The at least one biological or physiological measuring device may connected to a signal receiving device by an electrical lead permanently attached to the catheter system.

The at least one diagnostic component may provide any useful information, such as information about metabolic, physiologic and/or anatomic status of a a patient.

The information from said at least one biological or physiological measuring device would ordinarily be received by a host computer connected to said device.

More than one component or sensing element or measuring device would be among components that provides information other than information from said at least one biological or physiological measuring device. All or most of that information should be received by a host computer to evaluate a treatment procedure or patient conditions around the locality oftreatment. The additional components may measure, for example, vital signs of a patient. Information from more than one information source may received by the host computer and a treatment planning and control algorithm could be present in said host computer to process that information from more than one source.

[0018] A method according to the invention for treating a patient according to a treatment plan could comprise inserting the catheter system the invention into a patient, delivering therapy to the patient through at least one lumen of said catheter system, taking biological or physiological measurements of tissue or fluids within the patient, reporting said information to a computer, and evaluating performance of the treatment plan with the computer based upon comparing said information to expected biological or physiological information. The method could include information relating to at least two different biological or physiological measurements being electrically transmitted to the computer for evaluating performance of the treatment plan. Upon evaluation of the performance of the treatment plan, the computer could indicate a) a deviation for a range of acceptable levels of performance ofthe treatment plan, and b) an alteration of an existing treatment plan is identified. The method could have the computer signal the catheter system to actively modify the existing treatment plan. The method could also include having the computer signal an operator to actively modify the existing treatment plan.

BRIEF DESCRIPTION OF THE DRAWINGS

[0019]

Figure 1 is a representation of a layout of one embodiment of a multi-lumen, multi-function catheter system disclosed by the present invention.

Figure 2 shows a cross-sectional view of one em-

bodiment of a multi-lumen catheter device.

[0020] The present invention has enabled the combination of multiple functions into a catheter or probe system, enabling the performance of complete procedures by catheter along with additional, multiple or complete capability for ancillary or essential analytical procedures, diagnostic procedures, quantitative and qualitative analyses, operational environmental determinations, and any other task or information providing mechanism that provides information useful to the operation procedure. For example, a catheter system according to the present invention may provide two, three, four or more separate and distinct functions that can be performed distally (at the site of the catheter) without the necessity for removal of distal elements or replacement ofthe catheter. Information from the distal location can then be transmitted to a proximal intelligence source (e. g., processor, microprocessor, computer, hardware, software, etc.) for reading, visualization, analyzing, comparing, evaluation, and the like. This information can then be used to evaluate the ongoing procedure on a periodic, episodic, near real time, or real time basis to suggestion continuation of the existing procedure or alteration of the procedure. For example, the catheter may have separate biological and physiological delivery and evaluation systems for *in vivo* activity during a procedure. This can be important as ambient or induced biological activity and ambient or induced physiological activity can have direct results on the efficacy of the treatment or may indicate problems with the procedure. Determination of the status of these activities can assist in the assurance that an optimal or satisfactory procedure is being performed, and suggest methodology on improving the procedure while it is being administered. Multiple procedures or ancillary procedures, and multiple forms of operation environment evaluations can be performed through a single catheter with a single insertion of a catheter, with many or all of the functional elements needed for the procedures originally delivered with the catheter insertion or fed through the catheter. For example, tissue can be removed from a surface, therapeutic material delivered to the site, and conditions monitored on a local level to assure that at least minimal performance or operation standards are being maintained within the operational environment. A prophetic example of a multiple function procedure supported by a catheter according to techniques of the invention would be treatment of an area of tissue in the cranium where infection has damaged tissue over a targetable surface area. A catheter would be designed to provide fiber optic viewing capability with a multiplicity of fiber optic viewing fibers (and an optional light piping fiber), an ablative or irrigating device to remove irreparably damaged surface tissue, a removal lumen would be provided to assist in the physical removal of detritus from the removed damaged tissue, a delivery lumen would provide therapeutic agent to assist in the rapid healing or protection of newly exposed tissue that had previously been under the damaged tissue, and a solid state (e. g., semiconductor) pH sensing element extending from its own lumen can assist in measuring real time pH in the region of the therapeutic material delivery to assure that the pH in the region does not vary to such a degree that would indicate some deviation from the desired rate of delivery or loss of fluid from the newly exposed tissue. Other sensing systems (e.g., pressure measuring, thermometric, chemometric, etc.) can also be present. These sensing systems would transmit electrical signals through conductive elements (e.g., lines, wires, coils, etc.) to reading or recording systems. This information, either directly from the electrical conductors or through the reading or recording systems, would be evaluated (either by an operator or by artificial intelligence) and the procedure evaluated (by an operator or computer) on the basis ofthe information provided. The evaluation, based on known parameters for measuring the compliance of the procedure to acceptable standards, would dictate or indicate continuation of the procedure, modification of the procedure, or cessation of the procedure.

[0021] Evaluation of the performance of the procedure by artificial intelligence (e.g., hardware, software, computer, processor, microprocessor, chips, circuit boards, and the like) can be performed by any acceptable format. Specific or modified programs (for individual patients, for ranges or parameters within operable conditions, or specifically identified conditions being treated) can be provided to the artificial intelligence that suggest or dictate the progression of the procedure depending upon the readings. Although some general programs for the procedures my be developed, the system is particularly useful for increased automation of procedures where unusual circumstances might be present, such as patients with particular toxicity sensitivities, patients with underlying conditions (e.g., Parkinsonism, Type I diabetes, alcoholism, drug dependency, PKU, allergies, and the like) or patients on separate drug therapies where changed conditions in their blood chemistry from the operational procedure could affect the underlying condition. The software for the operational procedure could include special commands and attributes for the unique conditions or patients undergoing the procedure. As local conditions that could contribute to complications in operations are presently not easily considered and measured on a real time basis, this type of procedure, and especially tailoring the software to procedures on patients with unique requirements provides a significant advance within the field. As an example of this, the pH level of patients suffering from long term drug dependency (including excessive alcohol use) may have blood pH levels that are not within a normally accepted range. As some drugs and therapies may have pH sensitivities themselves, and the therapy may itself alter local pH even further, special modifications in the rates and/or concentrations of delivery may have to be modified in the program for a particular patient. A stand-

ard software procedure for otherwise healthy patients would not consider this underlying condition, even to the extent that a modification suggested by the 'normal' program could worsen the procedure under the special conditions of the underlying condition.

[0022] Figure 1 is a representation of a layout of one embodiment of a multi-lumen, multi-function catheter system disclosed as an aspect of the present invention. The catheter superstructure or manifold **2** comprises an external guide-tube **4** that contains the six individual internal lumens **6, 8, 10, 12, 14** and **16** of the catheter, or of a skeleton-like framework (shaped in cross section like a star washer) to which are affixed the individual lumens, including the central barrel **20** of the catheter. (Some specific configurations of the assembly of lumens that formulate the catheter are described later in Figure 2.) There may be several such individual lumens (for instance, up to "n" of the type of internal lumens such as **6, 8, 10, 12, 14** and **16)** inside of or otherwise integral to (e.g., distinct, self-supporting extruded tubes carried on an exterior surface or interior surface) the overall device. Some of the internal lumens can be configured as microdialysis devices, e.g., designed to sample the interstitial fluids. Other internal lumens might be infusion probes or drug delivery membranes. An online, real-time assessment of the dialysates gathered by such microdialysis devices can be accomplished by a variety of methods and systems that might range from microscale liquid chromatograph systems that are part of the physical structure of the device, to sophisticated, standalone genetic material analyzers and processors. Concurrently with the microdialysis analyses, a data acquisition system **24** can be added when needed to read in obtained and transmitted signals. The signals may be transported to the data acquisition system **24,** for example, through a lead wire **26.** That lead wire **26** is connected to a conductive element **28** embedded or affixed to the surface **30** ofthe guide tube **4.** The conductive element **30** is electrically connected at a distal end **32** to a contact plate **34.** The contact plate **34** is provided so that any functional device or microcatheter (not shown) can be electrically connected to the data acquisition system **24** easily, merely by being in electrical contact with the contact plate **34.** In this manner, a multi-probe component (a component catheter) ofthe system could be produced as a catheter, and a selection of electrically driven or signaling elements may be inserted into the component catheter. Snaps and other securing fitting may be provided, and these snaps and fittings may themselves be remotely controlled to secure and then release specific lumen fed devices on the catheter. Where there are both active and signaling functions within a single lumen (as in **6**), there may be multiple electrical leads **38** and **40.** There may be three, four or more electrical leads at each lumen, as is needed. These electrical leads may be manufactured by any convenient manner such as microlithographic etching of a metal coating into a circuit or conductor pattern, extruding conductors along with the extrusion of the guide tube **4,** and the like. The availability of multiple electrical leads **38** and **40** allows for the possibility of systems wherein at a single lumen, a device may be secured, released, activated, signaled to, signaled from, and programmed (if it contains memory). This offers unique functional capability to the system and the ability of the operator to control the local events of a procedure.

[0023] Figure 2 shows a cross-section of a multi-probe catheter **60** of the invention. A central barrel **64** is shown carrying a microcatheter **66** that can deliver material within a patient. Lumen **68** is shown carrying a solid state sensor **70** with an electrical conductor **72** carrying away signals. Another lumen **74** is shown carrying away a sampling tube **76.** A third lumen **78** is shown carrying an abrading tip **80** that may be distally or remotely controlled. A fourth lumen **82** carries a pH sensor **84** which is electrically connected to a conductor or wire **86** that carries signals from the pH sensor **84** to a computer (not shown). It is to be noted that lumens may be of different diameters, unevenly distributed, and as with lumen **88,** may be located outside of the main surface **90** of the catheter **60.**

The lumens, or at least some of the lumens, may carry vital signs sensors (e.g., pH sensors, pulse sensors, electrolyte concentration sensors, pressure sensors, specific solute sensors and any other type of medical monitors) that might be needed or desirable to successfully treat the patient. The data collection acquisition device **24** (e.g., a host computer) may collect and process these data via a treatment planning algorithm that the patient=s physician deems appropriate for the therapy being given, such as, for example the delivery of electrostimulation via a probe (not shown) through lumen **8** within the central barrel **20** of the catheter **2.** The strength of the stimulation signal can be regulated a controller upon instruction from the host computer or the computer can directly institute a modification ofthe procedure, particularly with coincident notification to the controller. An infusion and dialysis drug delivery controller electrically connected to the computer or manually operated can also be used to regulate the influx of drugs or other therapeutic agents into the patient via syringe drivers and infusion and output dialysis membrane probes passed through other available lumens (e.g., **10** and **12**) in the catheter **2** . In other embodiments of this invention, the treatment planning process might be carried out by the physician without recourse to an automated mechanism (computer, etc.). In such circumstances, the physician or therapist could simply monitor the results of the dialysis process and manually regulate the flow rates, pressures, and other variables of the infusion, dialysis drug-delivery, and electrostimulation processes. In still other embodiments of this invention, the computer and possibly other components of the therapy control system can be located at a remote site, perhaps a hospital or a care-provider=s office. The input and output signals to and from the therapy control sys-

tem can be mediated via transmission over wired or wireless telephone systems or by other types of data telemetry including satellite-based and other kinds of telemedicine linkages. As shown in Figure 1, individual lumens can be made in a variety of sizes to suit the application at hand for each of them. They might also have a variety of different port structures, for microdialysis, infusion. and other therapy delivery techniques.

[0024] One embodiment of the present invention also may comprise an integrated electronic personal health care monitoring system. The personal health care system center could comprise, for example, a computer for receiving or acquiring, storing, processing, and transmitting information, and a plurality of interfacing ports. Each interfacing port is adapted to accept a plurality of different patient monitoring modules, a plurality of different accessory modules for transactions, and a plurality of other interactive modules. Each module would be electrically interconnected to the data processor via the computer=s bus to exchange information with the computer=s CPU. The data processor includes means for providing operating instructions to the sensor modules, accessory modules, and therapy-providing modules. Each module provides information on a condition or vital sign of the patient. The data processor monitors the information provided by the modules and would act on it via an algorithm run by the computer.

[0025] The specific design of any feedback system disclosed by the present invention will depend on the application for which it is to be used. In general, it will have the arrangement shown in Figure 1. Dialysates sampled by the microdialysis probes will be analyzed by an online monitor, and the resulting data (following the necessary signal conditioning and, where appropriate, analog-to-digital conversion) will be input to a dedicated computer (CPU) that can also monitor the patient's vital signs, ICP readings, etc. The CPU can use any of a number of different feedback and control algorithms ("Patient Treatment Plans" or PTPs) selected by the physician as being the most appropriate for the needs of the patient at the time oftreatment. Such PTPs might incorporate straightforward PID laws or any other feedback control mechanism that effectively regulates drug delivery and electrostimulation levels as needed. In the method of the invention, the CPU that processes the feedback control mechanism can be in the patient's home, at the hospital bedside, in the physician's office, or at a location remote to the patient. In the latter case, given that the data rates for most physiological processes can be made slow, it would be possible to transmit / receive information to/from the processing computer using either ground-based or cellular phone systems and a modem. Thus, in a preferred embodiment of the invention, a physician or other appropriate health care professional can monitor and adjust the therapy provided to the patient, eg., the stimulation level, drug delivery rate, etc., via a telemedicine link, rather than requiring a visit by the patient to a conventional clinical care setting.

[0026] The system may include testing and measuring instruments to monitor the patient=s vital physiologic information, and may be adapted to a home healthcare and maintenance environment, even on a specific (unique) patient basis. The system may further include control devices having health care and maintenance functions monitored by the testing and measuring instruments in the system. In one embodiment wherein the system is arranged in the centralized network configuration, the testing and measuring instruments and the control devices are connected via a local area network with a data controller wherein all the vital information obtained in the system is stored. Instruments and devices are permitted controlled access to the controller through the network to retrieve necessary vital information therefrom. In another embodiment, the system is arranged in the distributed network configuration, with the vital information obtained by respective measuring instruments stored therein.

[0027] Figure 2 shows two examples of cross-sectional views of an actual multi-lumen multi-function catheter device. Each of the lumens has nominally the same internal diameter, although they can be of different internal diameters, as dictated by design considerations. The central barrel **52** of the catheter contains an electrostimulation lead **50** centered within it. The structural elements **53** keep the individual internal lumens **54, 56, 58,** and **60** and the central barrel from collapsing upon each other during catheter insertion, withdrawal, or during use.

[0028] These techniques may be used alone or in combination with the techniques described in U.S. Pat. No. 6,026,316 wherein problems, such as the following are addressed by real time or near real time observation of material concentration changes are observed by MR imaging techniques and acted upon after observation. One ofthe significant difficulties with delivery of materials such as drugs, hormones, or neurotransmitters to living tissue is assuring that the materials are delivered to the target receptor location in the intended amount. Many materials which are delivered to a patient, even though beneficial in the treatment of a specific condition, may be moderately or even strongly noxious or damaging to healthy tissue. It is therefore one object of conventional materials application treatment to maximize dosage to a desired location and to minimize dosage to locations which do not require the delivery of the material. Additionally, newer medical treatments may include procedures which remove unwanted deposits of materials with an expectation that the removal will be assisted by physical removal (by a withdrawal system) or natural bodily function removal (e.g., the circulatory system), or which may attempt to stimulate the body to produce natural chemicals (of which a patient may be deficient) at an increased rate (e.g., electrical stimulation to increase the production of dopamine). Because these procedures are usually highly invasive, it would be extremely

desirable to have a real time indication of immediate, transient and persistent effectiveness of the procedure. Where undesired deposits or collections of materials are being dispersed, it would be desirable to visualize the actual movement of materials to assist in collecting them (e.g., through catheters) or tracking them to assure that they are not again depositing or collecting (as in intravenous or cerebrospinal fluid blockage), or moving in segments which are too large and could cause blockage in other parts of the body as they are carried about. Unfortunately, with *in vivo* delivery of materials, particularly extremely small doses in small volumes delivered by small instrumentation into tissue regions protected by the blood-brain barrier, or the brain-cerebrospinal fluid barrier, or into visually inaccessible areas, it has not been possible to observe real time distribution of the material delivery, or the dispersion or distribution of the material at the injection or infusion site within the tissue. Where even small variations or miscalculations about the location of the target sight and the delivery device can significantly affect the delivery of material and the effectiveness of the delivered material, real time observation of the material delivery is even more critical than in topical or gross (e.g., massive systemic injection) delivery events. There has been no truly effective observation system for such delivery prior to the invention of U.S. Patent No. 6,026,316, which specification is incorporated herein, in its entirety, by reference.

[0029] The basic operation of the U.S. Patent No. 6,026,316 involves the initial MR imaging observation of a molecular environment of a patient (e.g., a particular area or region of a patient, such as tissue, particularly such tissue as that present in organs or systems of animal bodies and especially the human body, including, but not limited to the intracranial compartment and the various anatomic regions of the brain, including the cerebral ventricles, cisterns, epidural and subdural spaces, sinuses, and blood vessels, the spinal cord, including disks, nerves and associated vascular system, the heart and the coronary vascular circulation, liver and the hepatic vascular circulation, kidney and the renal vascular circulation, spleen and the splenic vascular system, gastrointestinal system, special senses, including the visual system, auditory system, and olfactory system endocrine system including the pituitary gland, thyroid gland, adrenal gland, testes, and ovaries, with observation of an MR image signal intensity at a given time and/or state (e.g., prior to material introduction or at some defined stage of material diffusion into the molecular environment In an example ofthe method of the invention, the distribution ofthe material in the tissue is determined by releasing an amount of the material through a drug delivery device positioned in the tissue, allowing the material to diffuse in the tissue, and analyzing the resulting MR signal intensity. On a continual basis or at some subsequent time interval later (e.g., a pulsed interval, preselected interval, random interval, frequent or sporadic intervals), the MR image of the molecular state within the same general area is observed. Changes in the characteristics, properties or quality of the image, such as the image signal intensity within the area are presumptively (and in most cases definitively) the result of the introduction of material into the original molecular environment and alteration of the MR response for regions of the environment where delivered material concentration has changed. By repeating observation of the MR image signal intensity within an area at least once (e.g., first taking the initial observation at a material concentration state at a time Ti, and at least one subsequent observation of MRI-observable changes such as in the signal intensity qualities at a time T2), the change in MR image signal intensity qualities can be related to the change in material concentration between times T, and T2, whether that change is from a starting point of zero concentration or from an existing concentration level. The observations therefore relate to the actual delivery of material into the molecular environment in an observable, and to some lesser degree, quantifiable manner.

[0030] A medical device used in the preferred practice ofthe present invention for delivery of materials may vary widely with respect to its structure, being highly dependent upon the particular procedural use to which it is being intended. However, there are many features which can be common to all of the devices or which should at least be considered in the various constructions. The simplest device could be a single delivery tube (catheter) having multiple lumens (of the same or different size), the catheter having MR responsive material in or on the composition ofthe tubing 19, preferably near the distal end or outlet of the delivery tube for assisting in detection by the MR imaging system. The next level of simplified construction would be the presence of MR coils or microcoils at or near the distal end of the catheter- This again, as elsewhere described, improves the visibility ofthe viewable signal observable by the MRI system. More than one coil or microcoil may be present, as the distribution of microcoils along a length of the catheter helps define the region within which local signals are detected at efficient intensities. As different medical procedures are performed in different environments, with different shapes and different variations in densities, the coils may be located, sized, angled, or otherwise designed to provide specific MR signals and/or responses tailored to the anticipated needs of a particular procedure. In general, the invention is best practiced by employing an array of RF microcoils, such that an image is obtained for any orientation of the drug delivery device.

[0031] The device may also include numerous catheter elements and/or ports and/or supplemental or independent functional elements. For example, at least two ports may be needed, one to carry in on chemical material, one to deliver a specific medical device or sensor and/or another port to deliver a second distinct chemical material which is or may become desirable during a medical procedure. For example, in addition to a primary

treatment chemistry being delivered, saline solutions or specifically tailored solutions to dilute potential oversized deliveries could be desirable. Some treatments may require sequences of drug delivery or delivery of various drugs which may not be storage stable prior to delivery to a patient. Separate ports would be desirable in those events. Additionally, ports may be used to evacuate undesirable materials directly or indirectly introduced by the medical procedure. A withdrawal port may comprise a tube with a port attached to negative pressure with respect to the opening in such a withdrawal port, thus being able to reduce liquid or small particle solids volumes within the area of the procedure. Where the liquid volume or solids are MR viewable, the MR viewable device may be directed towards specific locations or areas and the ports targeted towards those specific areas. In addition, the various ports may be marked or designed to provide distinct signals when viewed by MR systems so that they may be distinguished during performance of the procedures. For example, MR insensitive materials may be used to line a port or materials with different distributions or intensities of MR response may be used in the various ports to differentiate the elements while being observed during performance of procedures. For example, where a withdrawal tube has openings through which materials may be withdrawn, the orientation ofthat opening within the device becomes important. By lining the edges of the opening with material having unique MR responsiveness within the device, the position and orientation of the opening can be readily determined. Particularly preferred is a 2,000-5,000 angstrom thick coating of MR-visible material along the distal shaft of the device.

[0032] Where multiple catheters or ports or functional elements are combined into a single device, the configuration of the different components should be tailored for a particular procedure. The different components may be associated by various orientations. An MR-visible guidewire may be inserted within the device to assist in positioning the device at a target anatomical location. Particularly preferred is a guidewire or other structural support made of Nitinol™ or other MR-compatible shape memory metal. This is the simplest geometry and provides for smallest diameter sizing of the device. Other configurations such as parallel alignment of the elements in a strip-like orientation, stacking of elements in rows and columns, or mixtures of these and other configurations may also be useful. Other elements which may be included within the device, in addition to or separate from the use of delivery and/or withdrawal tubes, include thermal elements (for providing heat), radiation carrying elements (e.g., ultraviolet radiation, visible radiation, infrared radiation, and even hard radiation carrying elements, such as optical fibers or other internal reflection radiation carrying systems), detection elements (e.g., pH indicators, electronic activity indicators, pressure detectors, ion detectors, thermal detectors, solid-state chemical/gas detectors, cryogenic delivery, sonic delivery systems (for sonic disruption of material), radiation delivery systems, light delivery devices (e.g., UV for treatment or stimulation, infrared for ablation), cell delivery mechanisms, nutrient delivery systems, implantation systems, robotic element delivery systems, etc.), and any other sensing, treatment or detection element which would be useful during medical procedures. These individual elements are each (preferably independently) extendable to permit optimal positioning within the tissue would be configured as desired or needed for the particular procedure intended for the device. Procedurally inert elements such as structural supports, reinforcing elements or coatings, back-up elements, and the like, may also be present within the device. Particularly preferred as structural supports or reinforcing elements are circumferential bands of Nitinol® or other MR-compatible shape memory metals which, when activated, can facilitate accurate directed placement of the functional tip of the device.

[0033] One type of configuration which is presently considered as the preferred embodiment of the invention is the use of a core of element(s) surrounded by a sheath or distribution of additional elements. A central core element my comprise a single tube for delivery of a material, a pair of tubes for delivery of two chemicals, a delivery and withdrawal tube, or a procedurally inert structural support element. Around the central core element may be disposed multiple additional elements, usually seeking as near to a circular distribution about the central core as geometries allow. The attempt at the circular distribution is primarily for purposes of optimizing a small size for the diameter of the article, and is not necessarily a functional aspect to the performance of the device. MR responsive materials, including MR microcoils, may be located within the central core, around the central core (beneath any next layering of elements), or over the elements surrounding the central core. Where one or more ofthe elements receive, transmit or are powered by electrical signals, it is desirable that these elements be electrically separated by either or both of physical separation or additional insulation to prevent mixing or cross-transmission of signals between the distinct elements. Carrying and withdrawing tubes (as well as other elements) may also secondary functions. For example, a carrying tube may be conductive (by being naturally conductive or by having a conductive coating in or outside of the tube) and the electrical connection may be associated with an electronic element or component at the distal end of the device. The tube may thereby act as a carrying tube and electrical connection to the electronic component or element. Structural or adhesive support materials between different elements may also provide such functions.

[0034] The various individual elements within the device must be structurally associated, especially away from the distal end, and during insertion, may need structural association at the distal end. The structural support or structural integrity may be provided by some

physical means of attaching the various elements. This may be done by adhesive materials between the individual elements (which adhesive should be MR compatible). fusion of the various elements, or by coextrusion of the tubes into a single unit (or single component of a multiple element device). The adhesive may be an organic or inorganic adhesive. The distal end of the device may have the ends of the elements temporarily or controllably bonded during insertion. This may be beneficial because it may be desirable to have the individual elements fan out or separate during a medical procedure, for example, as in the case of a target tissue or area of pathology that is anatomically extensive. The adhesive could be water soluble (which would dissolve in a timely manner after insertion), solvent soluble (with solvent delivered into the distal end during a preliminary procedure, or radiation disruptable (e.g., a positive-acting resist adhesive composition which is sensitive to UV, visible or IR radiation which may be delivered through a radiation carrying port). Many other variations and combinations of these considerations and constructions may be used within the practice of the present invention. lin another embodiment the dialysis probe is replaced by an MR-visiblc microcatheter, which is a single extrusion catheter made from one of several possible sizes of a polyethylene terephthalate proximal shaft. A 12 mm distal segment of the microcatheter drug delivery device is made of elastomeric hydrogel or similar soft material which minimizes tissue damage during insertion. A plurality of semipermeable membranes are placed circumferentially at regular intervals along the distal segment of the microcatheter, thus enabling wide dispersion of an injected agent, semipermeable membrane consisting of a 0. 1 8-0.22 ml millipore filter. The companion microguidewire in this example is made ofNitinol or similar memory metal which enables directed placement of the tip of the catheter. A microguidewire may be threaded into a clear hub luek-lock cap made of poly-methelpentene or similar MR-compatible plastic. Both the catheter and guidewire have a linearly arranged array of radiopaque and MR-visible markers disposed at the distal end to provide easily identifiable reference points for trackability and localization under MR imaging and X-ray fluoroscopy guidance. The microcatheter can also be made from any of the well known soft, biocompatible plastics used in the catheter art such as Percuflex, a trademarked plastic manufactured by Boston Scientific Corporation of Watertown, Massachusetts. When the delivery device is positioned intracranially, the distal markers will be identifiable in an MR image and by X-rays. In another preferred embodiment, two or more R-F microcoils are placed along thc distal shaft of the m icrocatheter.

[0035] The delivery device can be employed to deliver pharmacologic therapies in order to reduce morbidity and mortality associated with cerebral ischemia, intracranial vasospasm, subarachnoid hemorrhage, and brain tumors. In the method of the invention the distal tip of the multi-lumen catheter assembly is typically positioned a few millimeters above the intracranial target structure using MR imaging. In one embodiment of the invention, surface modifications ofthe material components ofthe dialysis probe enable timed-release kinetics of MR-visible biologic response modifiers, including peptide macromolecules. In another embodiment of the invention, a pump or other infusion or injection device circulates a solution containing a therapeutic drug or an MR-visible contrast agent through the walls of the dialysis fiber into the brain at rates between 0.01 microliter/min to 10 microliter/min. In another preferred embodiment of the invention, pressure ejection techniques well described in the medical literature are used to deliver a predetermined amount of a therapeutic drug agent or MR-visible contrast through one or more of the tubular components of the multi-lumen device. In one specific preferred embodiment of the invention, the catheter is backfilled with the drug or contrast agent, which is functionally connected to a Picospritzer™ (General Valve Corp, Fairfield, NJ) or a similar instrument that is able to deliver pulses of nitrogen or compressed air with a duration ranging from a few milliseconds to several seconds at a pressure of 10-50 psi. Using such a pressure ejection mode of drug delivery, the concentration of the released substance in the vicinity of the tip is accurately defined by the concentration of the material in the delivery device. A binary solution can also be released, in that two therapeutic or diagnostic compounds can be delivered at the same time by pressure ejection of two materials from two or more separate microcatheters. Any material delivery system may be used in combination with the multiprobe catheter system of the invention. The material delivery device, for example, may comprise at least one device selected from the group consisting of:

A) a catheter assembly comprising at least two lumens;
B) a catheter assembly of from 2 to 10 mass transporting elements;
C) at least one light carrying element connected to a light reading system so that light projected into said area provides a signal through said light carrying device to said light reading system;
D) a light transmitting element associated with said material delivery device;
E) at least one thermally responsive element connected to a reading system for said thermal response so that temperatures or temperature changes within said area provide a signal to said reading system for said thermal response.

[0036] The system may contain an element capable of providing a charge is part of said material delivery device, said charge when provided being at a location on said material delivery device which assists in orienting of ionic material being delivered by said material de-

livery device within an area electrostatically near a point of release of said material from said material delivery device. The charge-providing element may, for example, be present to deliver electrical charge onto said material delivery device electrostatically near a point of release of said material from said material delivery device. The method may include observing the increase of material within aqueous environments or tissue in a living patient comprising the steps of:

a) observing by Magnetic Resonance Imaging a visible image within an area or volume comprising tissue of a living patient, said area or volume including a medical device which can be observed by Magnetic Resonance Imaging,
b) causing by said medical device at least some material which causes an alteration in the magnetic response of water in which said material is dispersed or dissolved to increase its concentration within said area or volume comprising an aqueous environment or tissue of a living patient,
c) observing a change in a property of said visible image of an area or volume comprising tissue of a living patient while said medical device is still present within said volume,
d) observing a change in a property of said visible image after said medical device has been moved from within said area or volume of tissue.

The medical device may stimulate a part of the patient to increase or decrease its production of a chemical whose presence in water causes a change in a property of said visible image. The method may include observing a different rate of passage of a chemical through structural material within the body of a living patient, said structural material having a delivery side and a distribution side, said method comprising the steps of:

a) observing by Magnetic Resonance Imaging a visible image within an area to volume comprising tissue of said living patient, said area or volume including a delivery device which can be observed by Magnetic Resonance Imaging,
b) causing by said delivery device to deliver at least some material which causes an alteration in the magnetic response of water in which said material is dispersed or dissolved,
c) observing movement of said material within said patient through said material from said delivery side to said distribution side,
d) observing a change in a property of a visible image in an area or volume on said distribution side of said material said medical device is still present within said area or volume, and
e) observing differences in rates of penetration of said chemical material through said structural material at different areas of said structural material which are indicative of different properties in said structural material at said different areas which are evidence of a clinical condition in said structural material. The changes in property of said visible image of an area or volume may, for example, comprise tissue of a living patient while said material delivery device is still present within said area or volume are caused by at least one change selected from the group consisting of:

a) a change in the apparent diffusion coefficient of tissue water protons;
b) a change in tissue magnetic susceptibility;
c) a change in T, tissue relativity;
d) a change in T2 tissue relativity;
e) a change in tissue magnetization transfer coefficients;
f) a change in tissue chemical shift frequency; and
g) a change in tissue temperature.

Claims

1. A multi-lumen, multi-functional catheter system comprising a plurality of axial lumens, at least one lumen supporting a functionality other than material delivery and material removal that results from the material delivery.

2. A catheter system as claimed in Claim 1 in which at least two individual lumens are parallel to a central barrel of the catheter.

3. A catheter system as claimed in Claim 1 or Claim 2 in which at least one of the at least two lumens is used for sampling fluids in a body part into which the catheter is inserted.

4. A catheter system as claimed in any preceding claim in which at least one of the axial lumens is used for infusion, injection or other mechanism of delivery of diagnostic and/or therapeutic agents into a body part in which the catheter is inserted.

5. A catheter system as claimed in any preceding claim in which a central lumen of the catheter contains an electrode.

6. A catheter system as claimed in Claim 5 wherein the electrode comprises a neurostimulator or radiofrequency-ablation lead.

7. A catheter system as claimed in any preceding claim in which an outer surface of the catheter comprises a continuous sheath inside of which are located at least three individual lumens, a central barrel between the three individual lumens and at least one medical treatment element other than material deliver and material delivery.

8. A catheter system as claimed in Claim 7 wherein at least one medical treatment element comprises an electrical lead.

9. A catheter system as claimed in any preceding claim wherein at least one biological or physiological measuring device is present within at least one lumen.

10. A catheter system as claimed in Claim 9 wherein said at least one biological or physiological measuring device is connected to a signal receiving device by an electrical lead associated with the catheter system.

11. A catheter system as claimed in any one of Claims 1 to 9 wherein at least one diagnostic component is present within or provided through at least one lumen and the at least one diagnostic component provides information about metabolic, physiologic and/or anatomic status of a patient.

12. A catheter system as claimed in Claim 11 wherein the at least one diagnostic component measures at least one vital sign of a patient.

13. A catheter system as claimed in any one of Claims 9 to 12 additionally comprising a computer to receive information from the at least one measuring device and/or the at least one diagnostic component.

14. A catheter system as claimed in Claim 13 additionally comprising a data transmission system connected to the catheter system wherein the data transmission system comprises a network selected from land line telephone, wireless telephone, direct wireless communication, fiber optic communication and telemetry.

15. A catheter system as claimed in any preceding claim which additionally comprises a central processing until, dynamic memory, static memory, a display device, input and output devices, mass storage devices, software, user interfaces, and user control devices.

16. A catheter system as claimed in any preceding claim comprising means for delivering therapy to the patient through at least one lumen of said catheter system and means taking biological or physiological measurements of tissue or fluids within the patient.

17. A catheter system as claimed in Claim 16 comprising a computer containing a program with a treatment planning and therapy delivery algorithm tailored to the needs of an individual patient and the program can be either adaptively adjusted by at least one controller selected from the computer itself as the therapy progresses, monitored by a remote station and adjusted by health care professionals, and by an automated system at the remote location, as the therapy progresses.

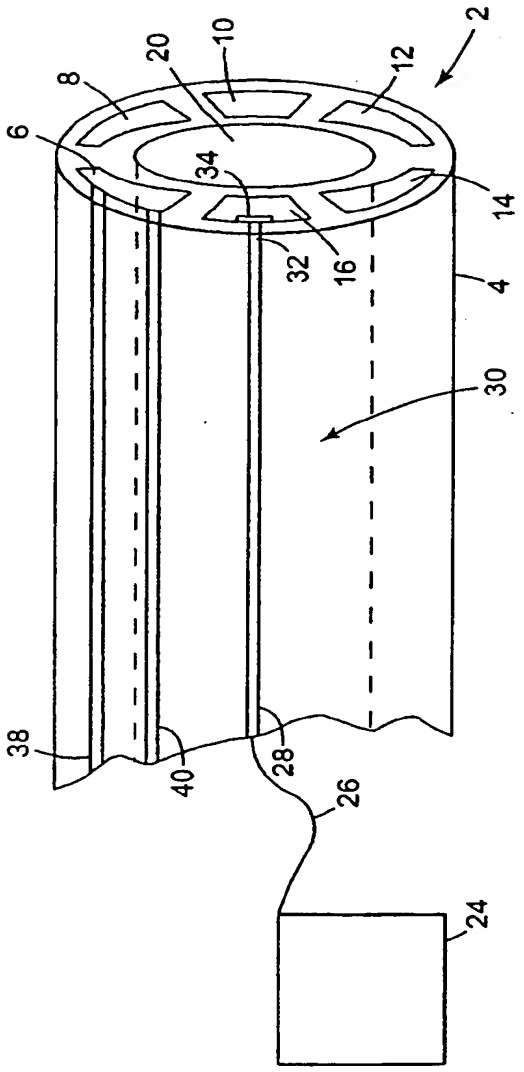

Fig. 1

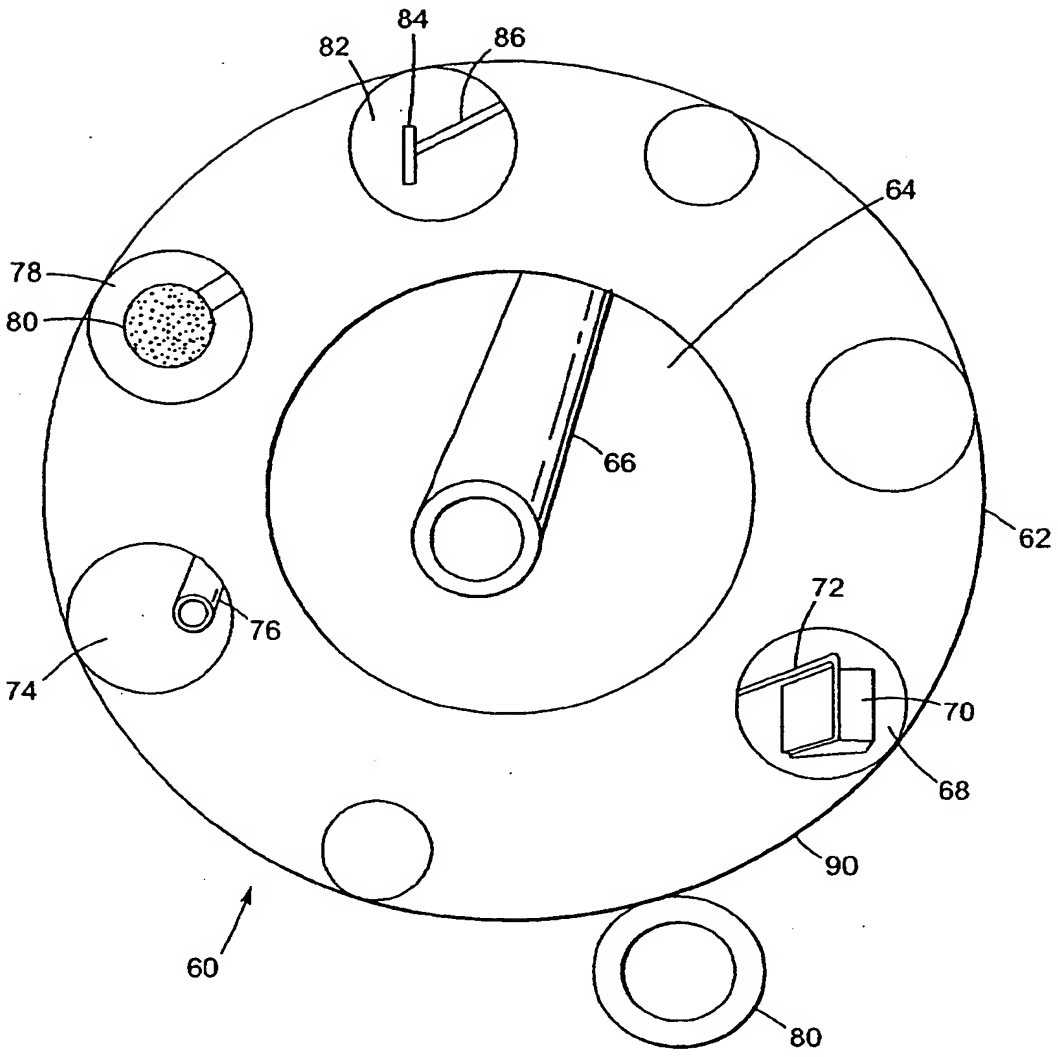

Fig. 2

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(54) **Multi-probe system**

(57) A multi-lumen, multi-functional catheter (2) system comprising a plurality of axial lumens (6,8,10,12,14,16), at least one lumen supporting a functionality other than material delivery and material removal.

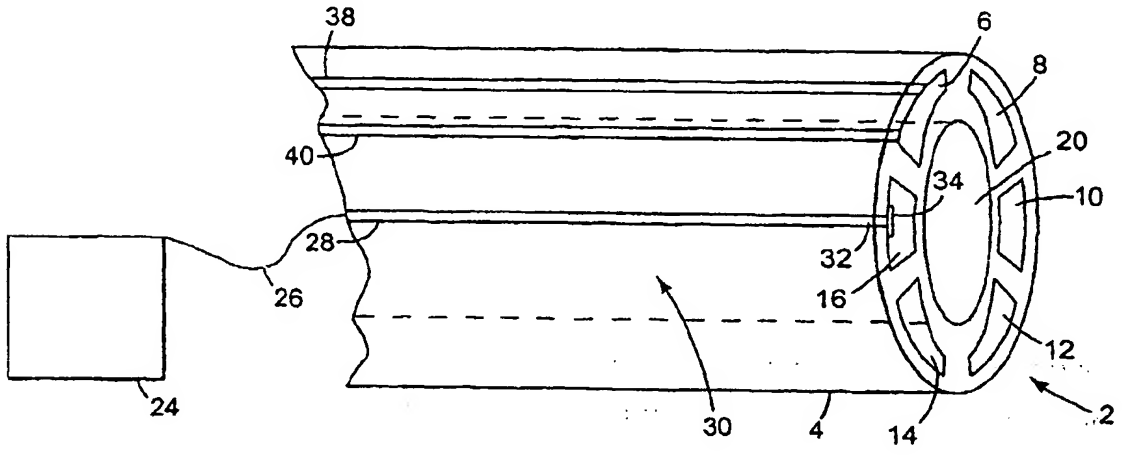

Fig. 1

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EUROPEAN SEARCH REPORT

Application Number
EP 01 30 3108

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Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
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The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
MUNICH	22 August 2002	Azaïzia, M

CATEGORY OF CITED DOCUMENTS

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ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 01 30 3108

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